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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,163	KAUVAR, LAWRENCE M.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-13 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledge Applicant's preliminary amendment filed 11/13/03, which cancelled claims 1-6 and 14-19. Currently, claims 7-13 and 20 are pending before the Office

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-13 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the preamble of the claim does not correlate with the outcome. For example, the preamble recites a method to obtain a database, while the final step recites recording observations in computer-readable and retrievable form. It is not clear how merely recording observations amounts to the creation of a database, absent a recitation of the elements, objects, or data structures comprising the database.

In claim 1, the recitation of "optionally as a function of time" with respect to "observing" and "recording" is indefinite because the progressive verbs "observing" and "recording" require a continuity of action.

In claim 20, the recitation of "useful" in the preamble is indefinite because a person of skill in the art would not know how to ascertain the standard or degree of usefulness required by "useful."

In claim 20, the recitation of "arbitrarily" in lines 4 and 6 is indefinite because a person of skill in the art would not know how to ascertain the standard or degree of arbitrariness required by "arbitrarily."

In claim 20, the recitation of "modify the status" in line 6 is indefinite because it is unclear what elements or characteristics are encompassed by "status" or how such elements or characteristics are modified.

In claim 20, the recitation of "said initial set of signal transduction proteins" in line 7 lacks antecedent basis.

In claim 20, the recitation of "provisional signal transduction proteins" in line 12 lacks antecedent basis.

In claim 20, the recitation of "a second set of proteins" in line 13 is indefinite because two sets of proteins have already been recited in prior steps.

In claim 20, the recitation of "principle components" in line 21 is indefinite because it is not clear what elements or characteristics are encompassed by "components" or how such elements or characteristics amount to a "principle" component.

In claim 20, the recitation of "the range" in line 21 lacks antecedent basis. Also, it is unclear what elements or characteristics comprise a "range."

In claim 20, the recitation of "marketed" in line 21 is indefinite because it is unclear how markets or marketing is incorporated into Applicant's invention.

In claim 20, two identical steps are recited in lines 8 and 17. In each step, intracellular localization information for the initial set of signal transduction proteins and compounds is compared. The purposes of these steps are unclear, as well as why these steps are performed twice on the initial set of signal transduction proteins and compounds.

Claim 20 is further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. An "additional set" of signal transduction proteins is recited in line 4. However, it is unclear how said "additional set" is incorporated into the method. Said "additional set" is recited only one time in the entire method, when it is arbitrarily identified in line 4, Said "additional set" does not appear to be used in any other steps of the method. Therefore, its function in the overall method is not clear, thereby rendering claim 20 indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use a database of signal transduction protein localization profiles.

The specification provides the general notion and potential uses of a database. For example, the specification teaches that intracellular signaling, such as PKC activity, provides an ideal basis for generating a broadly useable database of toxicity profiles (see Specification, p. 4-5). The specification continues to teach that such a database could be created so that testing an individual compound with respect to its effect on PKC isoenzyme intracellular localization can serve as a surrogate for evaluating not only whether or not it is toxic, but the nature of its toxicity see Specification, p. 5, lines 6-10). Such statements of intended, future use occur throughout the specification.

The specification does not teach the design and implementation of any database. Although the specification give reference to the type of information stored in a hypothetical database, no reference is given to any database design or functional characteristics of such a proposed database.

According to Arya et al., 20 COMPUT. MED. IMAGING. GRAPH. 269 (1996), a number of design consideration must be considered when developing a suitable database system. These considerations include: (1) query capability, (2) data characteristics, (3) logic design, and (4) physical database design. In addition, performance experiments should be performed to identify system bottlenecks.

The specification lacks any teaching on the design, functional characteristics, and implementation of any database, and whether any consideration was given to the query capability, data characteristics, logic design, or physical database design of the claimed database, or whether any system performance experiments were performed. Because the specification lacks a description or a working example of the claimed database, or direction as to its creation, and the quantity of experimentation needed to make and use a database, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 9-10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerdes & Kaether, 389 FEBS LETTERS 44 (1996).

Gerdes & Kaether describe a method to obtain a database (see p. 47, col. 1, "[http://www.comet.chr.va.us/quill/]" and "[http://www.cooperlab.wustl.edu/]") of signal transduction protein localization profiles (see ABSTRACT, "GFP can be used to localize proteins, to follow their movement...") in response to toxic compounds (see p. 45, col. 1, "cAMP-stimulated", p. 46, col. 2, "insulin-stimulated") comprising the steps of contacting a multiplicity of toxic compounds (see p. 45, col. 1, "cAMP-stimulated", p. 46, col. 2, "insulin-stimulated") with at least one cell type (see *e.g.* p. 45, col. 1, "*Dictyostelium*"), observing and recording (see p. 45, col. 1, "Real-time recordings") any translocation of at least one signal transduction protein (see *e.g.* p. 45, col. 1, "coronin", Table 1, "Fusion partner") in the presence of each toxic compound (see p. 45, col. 1, "cAMP-stimulated", p. 46, col. 2, "insulin-stimulated") as a function of time (see p. 45, col. 1, "Real-time recordings"), wherein at least 2 cell types are employed (See *e.g.* Table 1, "*Dictyostelium*" and "*S. cerevisae*"), the translocation of at least 2 signal transduction proteins is observed (See e.g. Table 1, "coronin" and "myosin"), and recording the observations of translocation (see p. 45, col. 1, "Real-time recordings") in computer-readable and retrievable form (see p. 47, col. 1, "[http://www.comet.chr.va.us/quill/]" and "[http://www.cooperlab.wustl.edu/]").

With respect to claim 9, the intracellular localization of at least two signal transduction proteins is determined (See e.g. Table 1, "coronin" and "myosin").

With respect to claim 10, the intracellular localization of a multiplicity of signal transduction proteins is determined (See e.g. Table 1, "coronin", "myosin", "Cap2p", "Exu", "tubulin", "MAP4", "Tau", "MP", "Nuf2", "S332", "hCgB", "KDELr", "HmgRp", "α1Pi", "TGN38", "Glut4", "hGH", "GAP", "Ras", "hGR", "rat glucocorticoid receptor", "H2B1", "Np13p", "nucleoplasmin", "Rev", "mitochondrial import signal of cytochrome c oxidase", "SKL").

With respect to claim 13, a computer-readable database is prepared (see p. 47, col. 1, "[http://www.comet.chr.va.us/quill/]" and "[http://www.cooperlab.wustl.edu/]").

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Sawin & Nurse, 94 PROC. NATL. ACAD. SCI. USA 15146 (1996).

Sawin & Nurse describe a method for screening a set of signal transduction proteins comprising the steps of arbitrarily identifying an additional set of signal transduction proteins (see p. 15146, col. 1, "A starting point... Burns et al., who identified open reading frames..."), determining the changes in intracellular localization (see e.g. Fig. 2) in response to an initial set of compounds (see p. 15146, col. 2, "pSGA genomic library") which modify the status of the intracellular environment (see e.g. Fig. 2), comparing the changes in intracellular localization (see p. 15147, col. 1, "colonies were screened by fluorescence microscopy") among members of the initial set of signal transduction proteins and compounds (see p. 15146, col. 2, "pSGA genomic library"), discarding signal transduction proteins which result in redundant translocation information (see

p. 15147, col. 2, "In a trial of ~384 colonies screened, 75 showed no fluorescence..."), substituting additional provisional signal transduction proteins and compounds (see p. 15147, col. 1, "rescreening of yeast") for the proteins and compounds discarded (see p. 15147, col. 2, "of ~384 colonies screened, 75 showed no fluorescence...") to obtain a second set of proteins (see Table 1, "Homologs") and a second set of compounds (see Table 1, "Plasmid"), obtaining intracellular localization information for the second set of compounds (see p. 15147, col. 1, "rescreening of yeast", Fig. 2), again comparing the intracellular localization information obtained among members of the initial set of signal transduction proteins and compounds (see p. 15147, col. 1, "rescreening of yeast", Fig. 2), discarding compounds and proteins that result in redundant profiles (see p. 15147, col. 1, "rescreening of yeast", Fig. 2), and repeating the foregoing steps (see p. 15147, col. 1, "rescreening of yeast") until a set of proteins is obtained (see Table 1, "Homologs") which provides at least five principle components (See DISCUSSION, "identified markers").

The language "with respect to the range of compounds marketed as small organic molecules" is interpreted as a statement of intended use and is not afforded patentable weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be

> patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerdes & Kaether, 389 FEBS LETTERS 44 (1996) in view of Mochly-Rosen, 268 SCIENCE 247 (1995).

Gerdes & Kaether describe a method to obtain a database of signal transduction protein localization profiles as described *supra*. Gerdes & Kaether also describe the use of GFP as a powerful tool for uncovering dynamic cellular events (see p. 47, col. 1), with few areas of biology onto which GFP could shed no light (see p. 47, col. 1).

Gerdes & Kaether do not teach a method incorporating protein kinase C (PKC). Also, Gerdes & Kaether do not teach a method incorporating the labeling of proteins with specific antibodies.

However, Mochly-Rosen teaches a method of observing the translocation of PKC (See *e.g.* Fig. 2) by using immunofluorescence (see p. 249, col. 3, line 2). The immunofluorescence studies of Mochly-Rosen necessarily contain an antibody, and would be so recognized by persons of ordinary skill in the art.

Therefore, it would have been obvious for a person of ordinary skill in the art to use the method of Gerdes & Kaether with PKC because both Gerdes & Kaether and Mochly-Rosen teach the use of GFP as a powerful tool for uncovering dynamic cellular events. Mochly-Rosen teaches that the localization of serine-threonine kinases through protein-protein interactions is an essential component of signal transduction and provides an important means of regulation (see p. 250, col. 3). Furthermore, Mochly-Rosen teaches that the localization of serine-threonine

kinases may be useful in the development of therapeutic agents (see ABSTRACT). Finally, both Gerdes & Kaether and Mochly-Rosen teach that such localization can be achieved through the use of GFP fusion proteins.

Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerdes & Kaether, 389 FEBS LETTERS 44 (1996) in view of Gerhard (US 5,684,628).

Gerdes & Kaether describe a method to obtain a database of signal transduction protein localization profiles as described *supra*. Gerdes & Kaether also teach that it is useful to display GFP data by video, and that future uses of GFP using FRET would open a new way for studying protein-protein interactions *in vivo* (see p. 47, col. 1).

Gerdes & Kaether do not teach the use of a wide-field microscope.

However, Gerhard teaches a wide-field microscope for illuminating biologically active samples (see col. 3, lines 29-31).

Therefore, it would have been obvious for a person of ordinary skill in the art to use the method of Gerdes & Kaether with a wide-field microscope, as taught by Gerhard, because Gerdes & Kaether teach the use of video to display data, and that future uses using FRET would open a new way for studying protein-protein interactions *in vivo* (see p. 47, col. 1). The use of video and FRET to display data can be provided by the time domain and optical frequency domain

imaging provided by Gerhard. Gerhard teaches that a wide-field microscope, along with conventional digital imaging and signal processing techniques, can be used to provide a three dimensional, time domain and optical frequency domain image of a biologically active specimen. Gerhard also teaches that such images are particularly valuable in the field of fluorescence microscopy where images of the specimen are not only integrated over time, but wavelength as well (see col. 1, lines 31-34).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

djv

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
8/9/04